Complete Summary

GUIDELINE TITLE

Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline.

BIBLIOGRAPHIC SOURCE(S)

The Endocrine Society. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Chevy Chase (MD): The Endocrine Society; 2007. 79 p. [281 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Thyroid dysfunction during pregnancy and postpartum including:

- Hypothyroidism
- Hyperthyroidism
- Gestational hyperemesis and hyperthyroidism
- Autoimmune thyroid disease
- Thyroid nodules and cancer
- Postpartum thyroiditis

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice
Obstetrics and Gynecology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide clinical guidelines for the management of thyroid problems present during pregnancy and in the postpartum

TARGET POPULATION

Pregnant women and women who are postpartum with thyroid dysfunction

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Management/Treatment

1. Targeted case finding of hypothyroidism at first prenatal visit
2. Adjustment of preconception thyroxine dose
3. Thyroid function testing
4. Differential diagnosis of hyperthyroidism
5. Antithyroid drug therapy
    - Propylthiouracil
    - Methimazole
6. Thyroidectomy
7. Measurement of thyroid receptor antibodies
8. Fetal ultrasound
9. Umbilical blood sampling, as appropriate
10. Assessment of newborns for thyroid dysfunction
11. Fine needle aspiration (FNA) cytology and ultrasound guided FNA
12. Thyroid hormone administration
13. Avoidance of radioactive iodine (RAI) and 131-I in pregnant women or women who are breast-feeding
14. Ensuring an adequate iodine intake
15. Measurement of urinary iodine concentration
16. Measurement of thyroid-stimulating hormone (TSH) levels in women known to be thyroid peroxidase antibody (TPO-Ab) positive
17. Postpartum screening for thyroiditis in women with type 1 diabetes mellitus
18. Annual TSH level in women with a history of postpartum thyroiditis (PPT)
19. Monitoring of TSH in asymptomatic women with an abnormal TSH who are not planning a subsequent pregnancy

20. Levothyroxine therapy for symptomatic women with an abnormal TSH who are planning pregnancy

MAJOR OUTCOMES CONSIDERED

- Risk for and prevalence of thyroid dysfunction in pregnancy and the postpartum period
- Incidence of fetal hyperthyroidism
- Incidence of miscarriage and preterm delivery
- Neuropsychological outcome of progeny
- Adverse effects of antithyroid drugs on fetal development and fetal thyroid

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The United States Preventive Services Task Force (USPSTF) grades the overall evidence for a service on a three-point scale (good, fair, or poor):

Good: Evidence includes consistent results from well designed, well conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

Level of Evidence by GRADE System

High: ++++ or +++O

Moderate: ++OO

Low: +OOO

Very Low: OOOO

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The guideline committee undertook to review all material on guideline topics published in English during the past two decades, or earlier at the working group's discretion. The committee concentrated on original reports and largely excluded reviews from their references. At present, with the exception of studies on iodide supplementation, only two prospective, randomized intervention trials have been published in this area. The guideline committee is aware of two large-scale prospective intervention trials that are presently ongoing. Nevertheless, in the last 15 years, many high-quality studies have modified older dogmas and profoundly changed the ways in which these patients are managed. These studies are most often prospective or retrospective clinical evaluations of a particular patient population and matched groups of control women. Such studies, when carefully performed, adequately matched, and appropriately interpreted; provide the bulk of the evidence presented in the guidelines.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

An international task force was created, under the auspices of The Endocrine Society, to review the best evidence in the field and develop evidence-based guidelines. Members of the task force included representatives from The Endocrine Society, American Thyroid Association, Association of American Clinical Endocrinologists, European Thyroid Association, Asia and Oceania Thyroid Association, and the Latin American Thyroid Society. The task force worked during 2 years to develop the guidelines, had multiple phone conversations, and two 2-day retreats. Upon completion of the guidelines, they were reviewed and approved by all of the participants.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The United States Preventive Services Task Force (USPSTF) grades its recommendations (level A, B, C, D or I) on the basis of the strength of evidence and magnitude of net benefits (benefits minus harms):

A: The USPSTF strongly recommends that clinicians provide (the service) to eligible patients. *The USPSTF found good evidence that (the service) improves important health outcomes and concludes that benefits substantially outweigh harms.*

B: The USPSTF recommends that clinicians provide (the service) to eligible patients. *The USPSTF found at least fair evidence that (the service) improves important health outcomes and concludes that benefits outweigh harms.*

C: The USPSTF makes no recommendation for or against routine provision of (the service). *The USPSTF found at least fair evidence that (the service) can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D: The USPSTF recommends against routinely providing (the service) to asymptomatic patients. *The USPSTF found good evidence that (the service) is ineffective or that harms outweigh benefits.*

I: The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing (the service). *Evidence that (the service) is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.*

Recommendation Level by GRADE System

1: Strong

2: Moderate

Note: There are no equivalents in the GRADE system for the recommendation levels C, D, and I used in the USPSTF system.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The manuscript was reviewed by the Society's Clinical Guideline's Subcommittee (CGS), Clinical Affairs Committee, members of The Endocrine Society, and members of each of the collaborating societies. Many valuable suggestions were

received and incorporated into the final document. Each of the societies endorsed the guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the quality of the evidence based on the United States Preventative Services Task Force [USPSTF] levels (good, fair, and poor) and Grading of Recommendations Assessment, Development and Evaluation [GRADE] levels (+OOO, ++OO, +++O, and ++++) and the strength of the recommendation (USPSTF: A, B, C, D, I and GRADE: 1 or 2) are provided at the end of the "Major Recommendations" field.

Hypothyroidism and Pregnancy: Maternal and Fetal Aspects

Both maternal and fetal hypothyroidism are known to have serious adverse effects on the fetus. Therefore maternal hypothyroidism should be avoided. For overt hypothyroidism (OH), The United States Preventive Service Task Force (USPSTF) recommendation level is A; evidence is fair. Targeted case finding is recommended at the first prenatal visit. The USPSTF recommendation level is B; evidence is fair (GRADE 2 | ++OO) (Abalovich et al., 2002; Klein et al., 1991; Haddow et al., 1999; Glinoer et al., 1994).

If hypothyroidism has been diagnosed before pregnancy, the guideline panel recommends adjustment of the preconception thyroxine dose to reach before pregnancy a thyroid-stimulating hormone (TSH) level not higher than 2.5 mIU/liter. The USPSTF recommendation level is I; evidence is poor (GRADE 2 | +OOO) (Demers & Spencer, 2002; Baloch et al., 2003; Panesar, Li, & Rogers, 2001).

The thyroxine dose often needs to be incremented by 4 to 6 weeks gestation and may require a 30 to 50% increment in dosage. The USPSTF recommendation level is A; evidence is good (GRADE 1 | +++O) (Mandel et al., 1990; Kaplan, 1992).

If OH is diagnosed during pregnancy, thyroid function tests should be normalized as rapidly as possible. Thyroxine dosage should be titrated to rapidly reach and thereafter maintain serum TSH concentrations of less than 2.5 mI/liter in the first trimester (or 3 mIU/liter in second and third trimesters) or to trimester-specific normal TSH ranges. Thyroid function tests should be remeasured within 30 to 40 days. The USPSTF recommendation level is A; evidence is good (GRADE 1 | ++++) (Soldin et al., 2004; Sapin, D'Herbomez, & Schlienger, 2004; Panesar, Li, & Rogers, 2001).

Women with thyroid autoimmunity (TAI) who are euthyroid in the early stages of pregnancy are at risk of developing hypothyroidism and should be monitored for elevation of TSH above the normal range. The USPSTF recommendation level is A; evidence is fair (GRADE 1 | +++O) (Alexander et al., 2004; Glinoer et al., 1994).

Subclinical hypothyroidism (SCH) (serum TSH concentration above the upper limit of the reference range with a normal free T_4) has been shown to be associated

with an adverse outcome for both the mother and offspring. Thyroxine treatment has been shown to improve obstetrical outcome, but has not been proved to modify long-term neurological development in the offspring. However, given that the potential benefits outweigh the potential risks, the panel recommends thyroxine replacement in women with subclinical hypothyroidism. For obstetrical outcome, the USPSTF recommendation level is B; evidence is fair (GRADE 1 | ++OO); for neurological outcome, the USPSTF recommendation level is I; evidence is poor (OOOO) (Abalovich et al., 2002; Leung et al., 1993; Casey et al., 2005; Glinoer, 1997).

After delivery, most hypothyroid women need to decrease the thyroxine dosage they received during pregnancy. The USPSTF recommendation level is A; evidence is good (GRADE 1 | ++++) (Caixas et al., 1999).

Management of Maternal Hyperthyroidism: Maternal Aspects

If a subnormal serum TSH concentration is detected during gestation, hyperthyroidism must be distinguished from both normal physiology of pregnancy and hyperemesis gravidarum because of the adverse effects of OH on the mother and fetus. Differentiation of Graves' disease from gestational thyrotoxicosis is supported by presence of clinical evidence of autoimmunity, a typical goiter, and presence of TSH-receptor antibodies (TRAb). The USPSTF recommendation level is A; evidence is good (GRADE 1 | ++++) (Mestman, 2004; Goodwin, Montoro, & Mestman, 1992; Tan et al., 2002; Davis et al., 1989; Millar et al., 1994).

For OH due to Graves' disease or thyroid nodules, antithyroid drug (ATD) therapy should be either initiated (for those with new diagnoses) or adjusted (for those with a prior history) to maintain the maternal thyroid hormone levels for free T4 in the upper nonpregnant reference range. The USPSTF recommendation level is A; evidence is good (GRADE 1 | ++++) (Momotani et al., 1986; Mortimer et al., 1990).

Because available evidence suggests that methimazole (MMI) may be associated with congenital anomalies, propylthiouracil (PTU) should be used as a first-line drug, if available, especially during first-trimester organogenesis. MMI may be prescribed if propylthiouracil is not available, or if a patient cannot tolerate or has an adverse response to propylthiouracil. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | ++OO) (Mandel, Brent, & Larsen, 1994; Martinez-Frias et al., 1992; Clementi et al., 1999; Johnsson, Larsson, & Ljunggren, 1997; Di Gianantonio et al., 2001; Greenberg, 1987; Wilson et al., 1998).

Subtotal thyroidectomy may be indicated during pregnancy as therapy for maternal Graves' disease if 1) a patient has a severe adverse reaction to ATD therapy, 2) persistently high doses of ATD are required, or 3) a patient is nonadherent to ATD therapy and has uncontrolled hyperthyroidism. The optimal timing of surgery is in the second trimester. The USPSTF recommendation level is I; evidence is poor (+OOO) (Stice et al., 1984; Burrow, 1985; Brodsky et al., 1980).

There is no evidence that treatment of subclinical hyperthyroidism improves pregnancy outcome, and treatment could potentially adversely affect fetal outcome. The USPSTF recommendation level is I; evidence is poor (+OOO)

(Goodwin, Montoro, & Mestman, 1992; Tan et al., 2002; Casey et al., 2006; Momotani et al., 1986).

Management of Maternal Hyperthyroidism: Fetal Aspects

Because thyroid receptor antibodies (thyroid receptor stimulating, binding, or inhibiting antibodies) freely cross the placenta and can stimulate the fetal thyroid, these antibodies should be measured by the end of the second trimester in mothers with current Graves' disease or with a history of Graves' disease and treatment with 131-I or thyroidectomy before pregnancy, or with a previous neonate with Graves' disease. Women who have a negative TSH-receptor antibodies (TRAb) and do not require ATD have a very low risk of fetal or neonatal thyroid dysfunction. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | +++O) (Nachum et al., 2003; Peleg et al., 2002; McKenzie & Zakarija, 1992; Laurberg et al., 1998; Luton et al., 2005).

131-I should not be given to a woman who is or may be pregnant. If inadvertently treated, the patient should be promptly informed of the radiation danger to the fetus, including thyroid destruction if treated after the 12th week of gestation. The USPSTF recommendation level is A; evidence is good (GRADE 1 | +OOO). There are no data for or against recommending termination of pregnancy after 131-I exposure. The USPSTF recommendation level is I; evidence is poor (+OOO) (Zanzonico, 1997; Berg et al., 1998; Lowe, 2004; Bydder et al., 2005; Gorman, 1999).

In women with elevated TRAb or in women treated with ATD, fetal ultrasound should be performed to look for evidence of fetal thyroid dysfunction, which could include growth restriction, hydrops, presence of goiter, advanced bone age, or cardiac failure. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | +++O) (Nachum et al., 2003; McKenzie & Zakarija, 1992; Laurberg et al., 1998; Mitsuda et al., 1992; Luton et al., 2005).

Umbilical blood sampling should be considered only if the diagnosis of fetal thyroid disease is not reasonably certain from the clinical data and the information gained would change the treatment. The USPSTF recommendation level is B; evidence is fair (GRADE 2 | +OOO) (Davidson et al., 1991; Nachum et al., 2003; Porreco & Bloch, 1990; Wenstrom et al., 1990; Cohen et al., 2003; Fisher, 1997; Polak et al., 1997; Wallace, Couch, & Ginsberg, 1995; Luton et al., 2005; Van Kamp et al., 2005; Polak et al., 2004).

All newborns of mothers with Graves' disease should be evaluated by a medical care provider for thyroid dysfunction and treated if necessary. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | +++O) (McKenzie & Zakarija, 1992, Mitsuda et al., 1992; Luton et al., 2005).

Gestational Hyperemesis and Hyperthyroidism

Thyroid function tests should be measured in all patients with hyperemesis gravidarum (5% weight loss, dehydration, and ketonuria). The USPSTF recommendation level is B; evidence is poor (GRADE 2 | +OOO) (Goodwin, Montoro, & Mestman, 1992; Tan et al., 2002; Goodwin et al., 1992; Lazarus, 2005).

Few women with hyperemesis gravidarum will require ATD treatment. The USPSTF recommendation level is A; evidence is good (GRADE 1 | ++++). Overt hyperthyroidism believed to be due to coincident Graves' disease should be treated with ATDs. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | ++OO). Gestational hyperthyroidism with clearly elevated thyroid hormone levels (free T_4 above the reference range or total T_4 >150% of top normal pregnancy value and TSH <0.1 microU/ml) and evidence of hyperthyroidism may require treatment as long as clinically necessary. The USPSTF recommendation level is I; evidence is poor (+OOO) (Goodwin, Montoro, & Mestman, 1992; Tan et al., 2002; Goodwin et al., 1992; Lazarus, 2005).

Autoimmune Thyroid Disease and Miscarriage

Although a positive association exists between the presence of thyroid antibodies and pregnancy loss, universal screening for antithyroid antibodies, and possible treatment, cannot be recommended at this time. As of this date, only one adequately designed intervention trial has demonstrated a decrease in the miscarriage rate in thyroid antibody-positive euthyroid women. The USPSTF recommendation level is C; evidence is fair (GRADE | +OOO) (Stagnaro-Green et al., 1990; De Carolis et al., 2004; Sher et al., 1998).

Thyroid Nodules and Cancer

Fine needle aspiration (FNA) cytology should be performed for single or dominant thyroid nodules larger than 1 cm discovered in pregnancy. Ultrasound guided FNA may have an advantage for minimizing inadequate sampling. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | +++O) (Kung et al., 2002; Mazzaferri & Jhiang, 1994; Moosa & Mazzaferri, 1997; Vini et al., 1999).

When nodules are discovered in the first or early second trimester to be malignant on cytopathological analysis or exhibit rapid growth, pregnancy should not be interrupted but surgery should be offered in the second trimester, before fetal viability. Women found to have cytology indicative of papillary cancer or follicular neoplasm without evidence of advanced disease, who prefer to wait until the postpartum period for definitive surgery, may be reassured that most well-differentiated thyroid cancers are slow growing and that surgical treatment soon after delivery is unlikely to change prognosis. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | ++OO) (Mazzaferri & Jhiang, 1994; Moosa & Mazzaferri, 1997; Vini et al., 1999; Herzon et al., 1994).

It is appropriate to administer thyroid hormone to achieve a suppressed but detectable TSH in pregnant women with a previously treated thyroid cancer, or a FNA positive for or suspicious for cancer, and those who elect to delay surgical treatment until postpartum. High-risk patients may benefit more from a greater degree of TSH suppression compared with low-risk patients. The free T_4 or total T_4 levels should ideally not be increased above the normal range for pregnancy. The USPSTF recommendation level is I; evidence is poor (+OOO) (Rosen, Korman, & Walfish, 1997).

Radioactive iodine (RAI) with 131-I should not be given to women who are breast-feeding. The USPSTF recommendation level is B; evidence is fair. Furthermore, pregnancy should be avoided for 6 months to 1 year in women with thyroid cancer

who receive therapeutic RAI doses to ensure stability of thyroid function, and confirm remission of thyroid cancer. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | ++OO) (Choe & McDougall, 1994; Schlumberger et al., 1995; Chow et al., 2004).

Iodine Nutrition during Pregnancy

Women in the childbearing age should have an average iodine intake of 150 micrograms/day. During pregnancy and breast-feeding, women should increase their daily iodine intake to 250 micrograms on average. The USPSTF recommendation level A; evidence is good (GRADE 1| +++O) (Glinoer, 2001; Glinoer, 2003; World Health Organization, 2005; Hollowell et al., 1998).

Iodine intake during pregnancy and breastfeeding should not exceed twice the daily recommended nutrient intake (RNI) for iodine (i.e. 500 micrograms iodine/day). The USPSTF recommendation level is I; evidence is poor (+OOO) (Glinoer, 2001; Glinoer, 2003; World Health Organization, 2005; Hollowell et al., 1998).

To assess the adequacy of the iodine intake during pregnancy in a population, urinary iodine concentration (UIC) should be measured in a representative cohort of the population. UIC should ideally range between 150 and 250 micrograms/liter. The USPSTF recommendation level A; evidence is good (GRADE 1 | ++++) (Delange, 2004).

To reach the daily RNI for iodine, multiple means must be considered, tailored to the iodine intake level in a given population. Different situations must therefore be distinguished: 1) countries with iodine sufficiency and/or with a well-established universal salt iodinization (USI) program, 2) countries without a USI program or with an established USI program where the coverage is known to be only partial, and 3) remote areas with no accessible USI program and difficult socioeconomic conditions. The USPSTF recommendation level is A; evidence is good (GRADE 1 | ++++) (Glinoer et al., 1995; Chaouki & Benmiloud, 1994; Liesenkotter et al., 1996; Nohr & Laurberg, 2000; Romano et al., 1991).

Postpartum Thyroiditis

There are insufficient data to recommend screening of all women for postpartum thyroiditis (PPT). The USPSTF recommendation level is I; evidence is poor (+OOO) (Stagnaro-Green, 2002; Muller, Drexhage, & Berghout, 2001).

Women known to be thyroid peroxidase antibody (TPO-Ab)-positive should have a TSH performed at 3 and 6 months postpartum. The USPSTF recommendation level is A; evidence is good (GRADE 1 | +++O) (Stagnaro-Green, 2002; Premawardhana et al., 2004).

The prevalence of PPT in women with type 1 diabetes mellitus (DM) is 3-fold greater than in the general population. Postpartum screening (TSH determination) is recommended for women with type 1 DM at 3 and 6 months postpartum. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | ++OO) (McCanlies et al., 1998; Alvarez-Marfany et al., 1994; Gerstein, 1993).

Women with a history of PPT have a markedly increased risk of developing permanent primary hypothyroidism in the 5-to 10-year period following the episode of PPT. An annual TSH level should be performed in these women. The USPSTF recommendation level is A; evidence is good (GRADE 1 | +++O) (Azizi, 2005; Othman et al., 1990; Premawardhana et al., 2000; Tachi et al., 1988).

Asymptomatic women with PPT who have a TSH above the reference range but less than 10 U/ml and who are not planning a subsequent pregnancy do not necessarily require intervention, but should, if untreated, be remonitored in 4 to 8 weeks. Symptomatic women and women with a TSH above normal and who are attempting pregnancy should be treated with levothyroxine. The USPSTF recommendation level is B; evidence is fair (GRADE 1 | ++OO) (Stagnaro-Green, 2002).

There is insufficient evidence to conclude whether an association exists between postpartum depression (PPD) and either PPT or thyroid antibody positivity (in women who did not develop PPT). The USPSTF recommendation level is I; evidence is poor (Kuijpens et al., 1998; Lucas et al., 2000; Cox, Murray, & Chapman, 1993; Stamp & Crowther, 1994; Harris et al., 1992; Pop et al., 1993). However, as hypothyroidism is a potentially reversible cause of depression, women with postpartum depression should be screened for hypothyroidism and appropriately treated. The USPSTF recommendation level is B; evidence is fair (GRADE 2 | ++OO) (Cleare et al., 1996).

Screening for Thyroid Dysfunction during Pregnancy

Although the benefits of universal screening for hypothyroidism may not be justified by current evidence, as presented in *Sections 1 to 7* in the original guideline document, we recommend case finding among the following groups of women at high risk for thyroid dysfunction:

1. Women with a history of hyperthyroid or hypothyroid disease, PPT, or thyroid lobectomy
2. Women with a family history of thyroid disease
3. Women with a goiter
4. Women with thyroid antibodies (when known)
5. Women with symptoms or clinical signs suggestive of thyroid underfunction or overfunction, including anemia, elevated cholesterol, and hyponatremia
6. Women with type I diabetes
7. Women with other autoimmune disorders
8. Women with infertility should have screening with TSH as part of their infertility work-up
9. Women with prior therapeutic head or neck irradiation
10. Women with a prior history of miscarriage or preterm delivery

The USPSTF recommendation level is B; evidence is fair (GRADE 1 | ++OO).

Definitions:

Strength of Evidence

The United States Preventive Services Task Force (USPSTF) grades the overall evidence for a service on a three-point scale (good, fair, or poor):

Good: Evidence includes consistent results from well designed, well conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

Strength of Recommendation

A: The USPSTF strongly recommends that clinicians provide (the service) to eligible patients. *The USPSTF found good evidence that (the service) improves important health outcomes and concludes that benefits substantially outweigh harms.*

B: The USPSTF recommends that clinicians provide (the service) to eligible patients. *The USPSTF found at least fair evidence that (the service) improves important health outcomes and concludes that benefits outweigh harms.*

C: The USPSTF makes no recommendation for or against routine provision of (the service). *The USPSTF found at least fair evidence that (the service) can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D: The USPSTF recommends against routinely providing (the service) to asymptomatic patients. *The USPSTF found good evidence that (the service) is ineffective or that harms outweigh benefits.*

I: The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing (the service). *Evidence that (the service) is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.*

Evidence Level by GRADE System

High: ++++ or +++O

Moderate: ++OO

Low: +OOO

Very Low: OOOO

Recommendation Level by GRADE System

1: Strong

2: Moderate

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and management of thyroid dysfunction during pregnancy and postpartum

POTENTIAL HARMS

- Subclinical hypothyroidism (SCH) (serum thyroid-stimulating hormone [TSH] concentration above the upper limit of the reference range with a normal free T4) has been shown to be associated with an adverse outcome for both the mother and offspring.
- Overtreatment of the mother with thioamides can result in iatrogenic fetal hypothyroidism.
- Treatment of maternal subclinical hyperthyroidism has not been found to improve pregnancy outcome and may risk unnecessary exposure of the fetus to antithyroid drugs (ATDs).
- There have been reports of two distinct teratogenic patterns associated with methimazole (MMI): aplasia cutis and choanal/esophageal atresia.
- Use of propranolol in late pregnancy has been associated with mild and transitory neonatal hypoglycemia, apnea, and bradycardia. Finally, there are case reports suggesting an association between propranolol use and intrauterine growth restriction, but this remains controversial.
- Fetal exposure to high doses of radiation before organogenesis (before 4 to 6 weeks gestation) can lead to miscarriage or have no effect. Radiation exposure later in gestation can be associated with malformations, growth restriction, developmental delay and induction of malignancies.

- Exposure after 12 weeks can induce thyroid ablation, requiring intrauterine thyroid hormone replacement and lifelong therapy for hypothyroidism.
- If surgery is elected in pregnancy, it is best avoided in the first and third trimester. During the first trimester, there is concern over the possible teratogenic effects on the fetus, and surgery of any type is associated with increased early fetal loss. Surgery of any type in the third trimester is associated with a higher incidence of preterm labor. For cancer found early in pregnancy, surgery during the second trimester before fetal viability (<22 weeks) appears safe for the patient and the fetus. Fetal loss has been reported only in association with extensive neck exploration.
- Excessive levels of iodine intake may potentially cause more disease. Furthermore, individuals must be identified who may have side effects from excessive iodine intake, such as patients with known or underlying autoimmune thyroid disorders or autonomous thyroid tissue.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Because the experience with iodides is more limited, iodides should not be used as a first-line therapy for women with Graves' disease, but they could be used transiently if needed in preparation for thyroidectomy.
- Radioactive iodine (RAI) diagnostic tests and therapy are contraindicated during pregnancy, and all women who could potentially become pregnant should have a pregnancy test before 131-I administration.
- In addition, 131-I is contraindicated in breast-feeding mothers, and breast-feeding should cease if the exposure is unavoidable.

QUALIFYING STATEMENTS

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- Clinical Practice Guidelines are developed to be of assistance to endocrinologists by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The Guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of healthcare providers and each patient's individual circumstances.
- The Endocrine Society makes no warranty, express or implied, regarding the Guidelines and specifically excludes any warranties of merchantability and fitness for a particular use or purpose. The Society shall not be liable for direct, indirect, special, incidental, or consequential damages related to the use of the information contained herein.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Foreign Language Translations
Patient Resources
Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

The Endocrine Society. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Chevy Chase (MD): The Endocrine Society; 2007. 79 p. [281 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007

GUIDELINE DEVELOPER(S)

The Endocrine Society - Disease Specific Society

SOURCE(S) OF FUNDING

The Endocrine Society

GUIDELINE COMMITTEE

Thyroid Dysfunction during Pregnancy and Postpartum Guideline Task Force

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: Marcos Abalovich; Nobuyuki Amino; Linda A. Barbour; Rhoda H. Cobin; Leslie J. De Groot; Daniel Glinoer; Susan J. Mandel; Alex Stagnaro-Green

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Leslie J. DeGroot, MD(chair) – Significant Financial Interests: None Declared; Governance: None Declared; Consultation or Advisement: Occasional consultant with Abbott Laboratories; Grant or Other Research Support: None Declared; Other: Grant support to Thyroidmanager.org Web site by Abbott Laboratories.

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American Thyroid Association - Professional Association
Asian & Oceania Thyroid Association - Disease Specific Society
European Thyroid Association - Disease Specific Society
Latin AmericanThyroid Association - Disease Specific Society

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society.

Print copies: Available from The Endocrine Society, c/o Bank of America, P.O. Box 630721, Baltimore, MD 21263-0736; Phone: (301) 941.0210; Email: Societyservices@endo-society.org

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Executive summary. 2007. 14 p. Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society.

Print copies: Available from The Endocrine Society, c/o Bank of America, P.O. Box 630721, Baltimore, MD 21263-0736; Phone: (301) 941.0210; Email: Societyservices@endo-society.org

PATIENT RESOURCES

The following are available:

- Patient guide on maternal thyroid nodules and cancer before, during, and after pregnancy. Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society. See the related QualityTool summary on the Health Care Innovations Exchange Web site.
- Patient guide to the management of maternal hyperthyroidism before, during and after pregnancy. Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society. See the related QualityTool summary on the Health Care Innovations Exchange Web site.
- Patient guide to the management of maternal hypothyroidism before, during and after pregnancy. Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society. See the related QualityTool summary on the Health Care Innovations Exchange Web site.
- Postpartum thyroiditis fact sheet. Electronic copies: Available in Spanish and English in Portable Document Format (PDF) from The Endocrine Society. See

the related QualityTool summary on the Health Care Innovations Exchange Web site.

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